

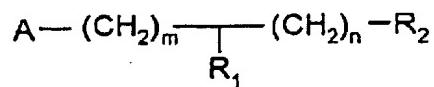
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Amendments to the Claims

JC17 Rec'd PCT/PTO 20 SEP 2005

Please amend the listing of claims as follows:

1. (Original) A compound of structural formula (I):



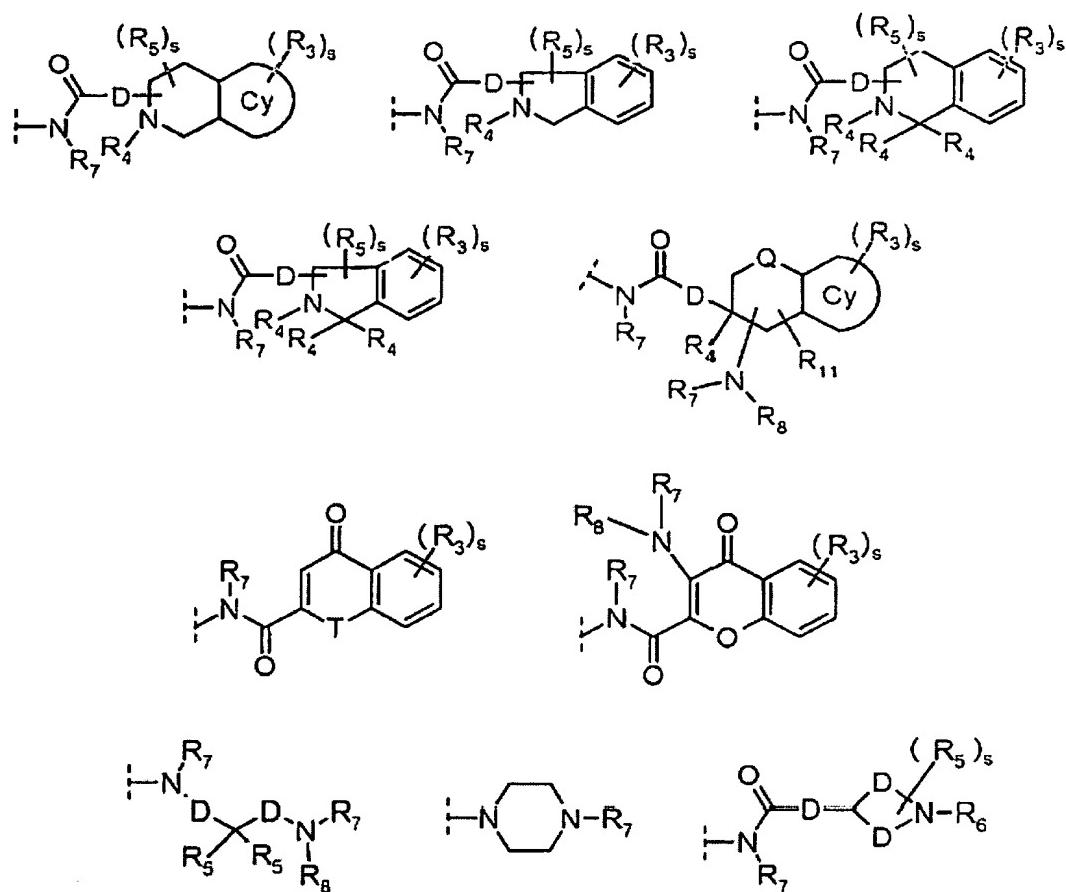
(I)

or a pharmaceutically acceptable salt or a solvate thereof, wherein

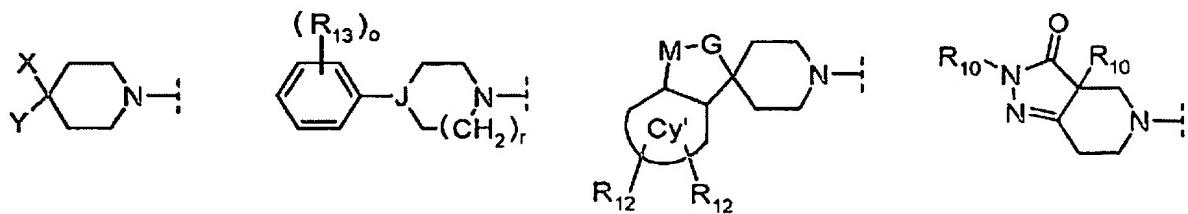
R<sub>1</sub> is:

(D)-aryl or (D)-heteroaryl,  
wherein aryl and heteroaryl are unsubstituted or substituted;

R<sub>2</sub> is:



A is:



each R<sub>3</sub> is independently:

hydrogen,  
halo,  
alkyl ,  
haloalkyl,  
hydroxy,  
alkoxy,  
S-alkyl,  
SO<sub>2</sub>-alkyl,  
O-alkenyl,  
S-alkenyl,  
NR<sub>15</sub>C(O)R<sub>15</sub>,  
NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub>,  
N(R<sub>15</sub>)<sub>2</sub>,  
(D)-cycloalkyl,  
(D)-aryl (wherein aryl is phenyl or naphthyl),  
(D)-heteroaryl,  
(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and  
wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted, and two adjacent R<sub>3</sub> may form a 4- to 7-membered ring;

each R<sub>4</sub> is independently:

hydrogen,  
alkyl,  
C(O)-alkyl,  
SO<sub>2</sub>alkyl,  
SO<sub>2</sub>aryl,  
(D)-aryl or  
(D)-cycloalkyl;

each R<sub>5</sub> is independently:

- hydrogen,
- alkyl,
- (D)-aryl,
- (D)-heteroaryl,
- (D)-N(R<sub>7</sub>)<sub>2</sub>,
- (D)-NR<sub>7</sub>C(O)-alkyl,
- (D)-NR<sub>7</sub>SO<sub>2</sub>-alkyl,
- (D)-SO<sub>2</sub>N(R<sub>7</sub>)<sub>2</sub>,
- (D)-(O)<sub>q</sub>-alkyl,
- (D)-(O)<sub>q</sub>(D)-NR<sub>7</sub>COR<sub>7</sub>,
- (D)-(O)<sub>q</sub>(D)- NR<sub>7</sub>SO<sub>2</sub>R<sub>7</sub>,
- (D)-(O)<sub>q</sub>-heterocyclyl or
- (D)-(O)<sub>q</sub>(alkyl)-heterocyclyl;

each R<sub>6</sub> is independently:

- hydrogen,
- alkyl,
- (D)-phenyl,
- C(O)-alkyl,
- C(O)-phenyl,
- SO<sub>2</sub>-alkyl or
- SO<sub>2</sub>-phenyl;

R<sub>7</sub> and R<sub>8</sub> are each independently:

- hydrogen,
- alkyl or
- (D)-cycloalkyl, or

R<sub>7</sub> and R<sub>8</sub> together with the nitrogen to which they are attached form a 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S and NR<sub>4</sub>,  
wherein alkyl and cycloalkyl are unsubstituted or substituted;

$R_{10}$  is independently:

hydrogen,  
alkyl,  
(D)-aryl or  
(D)-cycloalkyl;

$R_{11}$  is:

hydrogen or  
alkyl;

$R_{12}$  is:

hydrogen,  
halo,  
alkyl,  
alkoxy,  
 $C \equiv N$ ,  
 $CF_3$  or  
 $OCF_3$ ;

$R_{13}$  is independently:

hydrogen,  
hydroxy,  
cyano,  
nitro,  
halo,  
alkyl,  
alkoxy,  
haloalkyl,  
(D)- $C(O)_{15}$ ,  
(D)- $C(O)_{15}$ ,  
(D)- $C(O)SR_{15}$ ,  
(D)- $C(O)$ -heteroaryl,  
(D)- $C(O)$ -heterocyclyl,  
(D)- $C(O)N(R_{15})_2$ ,

(D)-N(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>COR<sub>15</sub>,  
(D)-NR<sub>15</sub>CON(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>C(O)OR<sub>15</sub>,  
(D)-NR<sub>15</sub>C(R<sub>15</sub>)=N(R<sub>15</sub>),  
(D)-NR<sub>15</sub>C(=NR<sub>15</sub>)N(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub>,  
(D)-NR<sub>15</sub>SO<sub>2</sub>N(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>(D)-heterocyclyl,  
(D)-NR<sub>15</sub>(D)-heteroaryl,  
(D)-OR<sub>15</sub>,  
OSO<sub>2</sub>R<sub>15</sub>,  
(D)-[O]<sub>q</sub>(cycloalkyl),  
(D)-[O]<sub>q</sub>(D)-aryl,  
(D)-[O]<sub>q</sub>(D)-heteroaryl,  
(D)-[O]<sub>q</sub>(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen when q=1),  
(D)-SR<sub>15</sub>,  
(D)-SOR<sub>15</sub>,  
(D)-SO<sub>2</sub>R<sub>15</sub> or  
(D)-SO<sub>2</sub>N(R<sub>15</sub>)<sub>2</sub>,  
wherein alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl and heteroaryl are unsubstituted or substituted;

each R<sub>15</sub> is independently:

hydrogen,  
alkyl,  
haloalkyl,  
(D)-cycloalkyl,  
(D)-aryl (wherein aryl is phenyl or naphthyl),  
(D)-heteroaryl,  
(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and

wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted;

R<sub>17</sub> is independently:

R<sub>10</sub> or  
(D)-heterocyclyl;

R<sub>18</sub> is independently:

R<sub>10</sub>,  
(D)-heteroaryl,  
(D)-heterocyclyl,  
(D)-N(Y)<sub>2</sub>,  
(D)-NH-heteroaryl or  
(D)-NH-heterocyclyl,  
wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted, or  
two R<sub>18</sub> groups together with the atoms to which they are attached form a 5- to 8-membered mono- or bi-cyclic ring system optionally containing an additional heteroatom selected from O, S, NR<sub>10</sub>, NBoc and NZ;

Cy is:

aryl,  
5- or 6-membered heteroaryl,  
5- or 6-membered heterocyclyl or  
5- or 7-membered carbocyclyl;

Cy' is:

benzene,  
pyridine or  
cyclohexane;

X is:

alkyl,  
(D)-cycloalkyl,

(D)-aryl,  
(D)-heteroaryl,  
(D)-heterocyclyl,  
(D)-C≡N,  
(D)-CON(R<sub>17</sub>R<sub>17</sub>),  
(D)-CO<sub>2</sub>R<sub>17</sub>,  
(D)-COR<sub>17</sub>,  
(D)-NR<sub>17</sub>C(O)R<sub>17</sub>,  
(D)-NR<sub>17</sub>CO<sub>2</sub>R<sub>17</sub>,  
(D)-NR<sub>17</sub>C(O)N(R<sub>17</sub>)<sub>2</sub>,  
(D)-NR<sub>17</sub>SO<sub>2</sub>R<sub>17</sub>,  
(D)-S(O)<sub>p</sub>R<sub>17</sub>,  
(D)-SO<sub>2</sub>N(R<sub>17</sub>)(R<sub>17</sub>),  
(D)-OR<sub>17</sub>,  
(D)-OC(O)R<sub>17</sub>,  
(D)-OC(O)OR<sub>17</sub>,  
(D)-OC(O)N(R<sub>17</sub>)<sub>2</sub>,  
(D)-N(R<sub>17</sub>)(R<sub>17</sub>) or  
(D)-NR<sub>17</sub>SO<sub>2</sub>N(R<sub>17</sub>)(R<sub>17</sub>),  
wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted;

Y is:

hydrogen,  
alkyl,  
(D)-cycloalkyl,  
(D)-aryl,  
(D)-heterocyclyl or  
(D)-heteroaryl,  
wherein aryl, heteroaryl, alkyl, D and cycloalkyl are unsubstituted or substituted;

Q is a bond, O, S(O)<sub>u</sub>, NR<sub>6</sub> or CH<sub>2</sub>;

D is a bond or C<sub>1</sub> - C<sub>4</sub> alkyl;

E is O, S or NR<sub>6</sub>;

G is D, CH-alkyl, O, C=O or SO<sub>2</sub>, with the proviso that when G is O, the ring atom M is carbon;

J is N or CH;

M is CHCO<sub>2</sub>Y, CHC(O)N(Y)<sub>2</sub>, NSO<sub>2</sub>R<sub>18</sub>, CHN(Y)COR<sub>18</sub>, CHN(Y)SO<sub>2</sub>R<sub>18</sub>, CHCH<sub>2</sub>OY or CHCH<sub>2</sub>heteroaryl;

T is O or NR<sub>7</sub>;

n is 0 - 3;

m is 1 - 3;

o is 0 - 3;

p is 0 - 2;

q is 0 or 1;

r is 1 or 2;

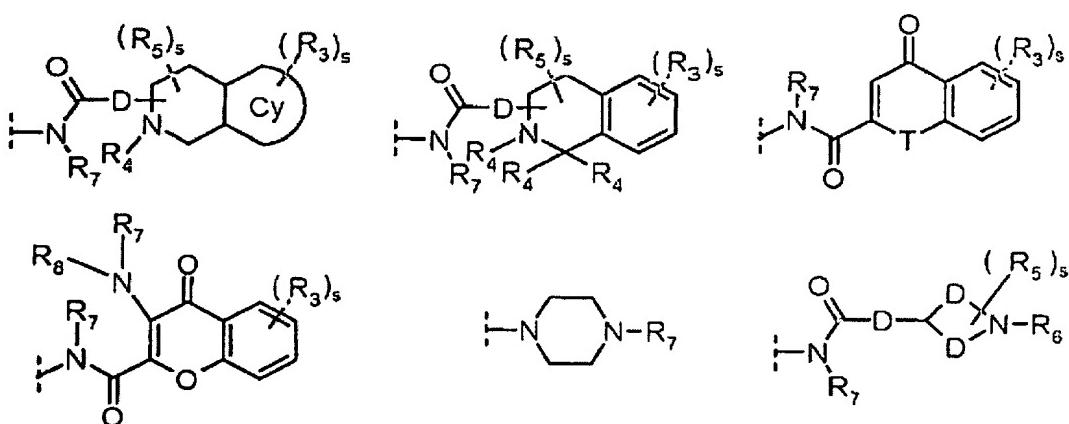
s is 0 - 3;

u is 0 - 2.

2. (Original) The compound of claim 1, wherein

R<sub>1</sub> is (D)-aryl which may be substituted with one to three substituents independently selected from the group consisting of cyano, nitro, perfluoroalkoxy, halo, alkyl (D)-cycloalkyl, alkoxy, hydroxy and haloalkyl;

R<sub>2</sub> is:



$R_3$  is independently:

- hydrogen,
- halo,
- alkyl,
- hydroxy,
- alkoxy,
- S-alkyl,
- $SO_2$ -alkyl,
- O-alkenyl,
- S-alkenyl,
- haloalkyl or
- (D)-cycloalkyl;

$R_4$  is:

- hydrogen or
- alkyl;

each  $R_5$  is independently:

- hydrogen,
- alkyl,
- (D)-aryl,
- (D)-heteroaryl,
- (D)- $N(R_7)_2$ ,
- (D)- $NR_7C(O)alkyl$  or
- (D)- $NR_7SO_2alkyl$ ;

$R_7$  and  $R_8$  are each independently:

- hydrogen,
- alkyl or
- cycloalkyl, or

$R_7$  and  $R_8$  together with the nitrogen to which they are attached form a 5- to 7-membered ring optionally containing an additional heteroatom selected from O, S and  $NR_4$ ;

$R_9$  is:

alkyl,  
 $OR_{10}$ ,  
(D)-aryl,  
(D)-cycloalkyl,  
(D)-heteroaryl and  
halo;

$R_{12}$  is:

hydrogen,  
halo,  
alkyl,  
alkoxy or  
 $C\equiv N$ ;

$R_{13}$  is independently:

hydrogen,  
hydroxy,  
cyano,  
nitro,  
halo,  
alkyl,  
alkoxy,  
haloalkyl,  
(D)-C(O)-heterocyclyl,  
(D)-N( $R_{15}$ )<sub>2</sub>,  
(D)-NR<sub>15</sub>COR<sub>15</sub>,  
(D)-NR<sub>15</sub>CON( $R_{15}$ )<sub>2</sub>,  
(D)-NR<sub>15</sub>C(O)OR<sub>15</sub>,  
(D)-NR<sub>15</sub>C( $R_{15}$ )=N( $R_{15}$ ),  
(D)-NR<sub>15</sub>C(=NR<sub>15</sub>)N( $R_{15}$ )<sub>2</sub>,  
(D)-NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub> or  
(D)-NR<sub>15</sub>SO<sub>2</sub>N( $R_{15}$ )<sub>2</sub>;

each R<sub>14</sub> is independently:

- hydrogen,
- halo,
- alkyl,
- (D)-cycloalkyl,
- alkoxy or
- phenyl;

each R<sub>15</sub> is independently:

- hydrogen,
- halo,
- alkyl,
- (D)-cycloalkyl,
- alkoxy or
- phenyl;

each R<sub>16</sub> is independently:

- hydrogen,
- alkyl or
- cycloalkyl;

X is:

- alkyl,
- (D)-cycloalkyl,
- (D)-aryl,
- (D)-heteroaryl,
- (D)-heterocyclyl,
- (D)-NHC(O)R<sub>17</sub>,
- (D)-CO<sub>2</sub>R<sub>17</sub> or
- (D)-CON(R<sub>17</sub>R<sub>17</sub>);

Y is:

- hydrogen,
- alkyl,

(D)-cycloalkyl,  
(D)-aryl,  
(D)-heterocyclyl or  
(D)-heteroaryl;

Cy is:

aryl,  
5- or 6-membered heteroaryl,  
5- or 6-membered heterocyclyl or  
5- to 7-membered carbocyclyl;

Cy' is benzene or pyridine;

D is a bond or C<sub>1</sub> - C<sub>4</sub>-alkylene;

M is NSO<sub>2</sub>R<sub>18</sub>, CHN(Y)COR<sub>18</sub> or CHN(Y)SO<sub>2</sub>R<sub>18</sub>;

G is D or CH-alkyl;

T is NR<sub>7</sub> or O;

n is 0 or 1 ;

m is 1 or 2;

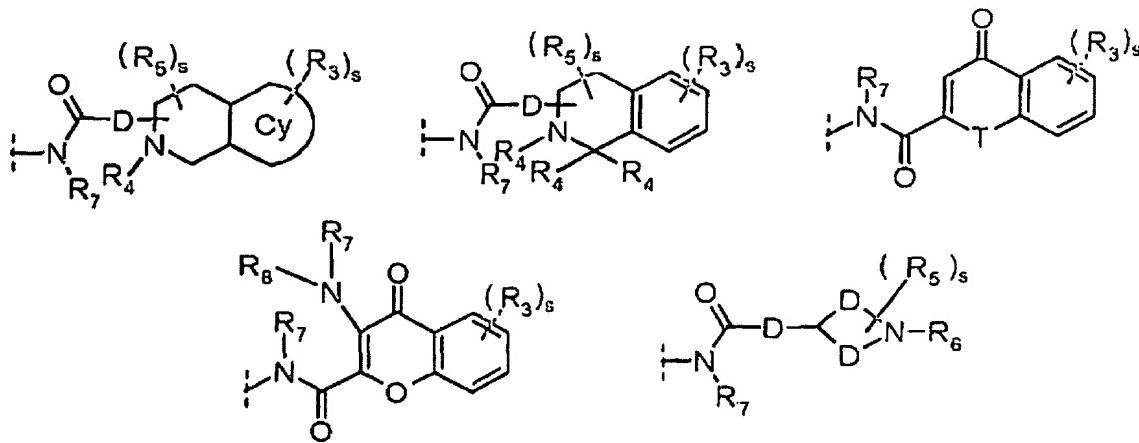
r is 1;

s is 0, 1 or 2.

3. (Currently Amended) The compound of ~~claims 1 or 2~~claim 1, wherein

R<sub>1</sub> is (D)-phenyl or (D)-naphthyl which may be substituted with one or two substituents independently selected from the group consisting of perfluoroalkoxy, halo, alkyl, alkoxy and haloalkyl;

$R_2$  is:



$R_3$  is hydrogen or halo;

$R_4$  is hydrogen;

$R_5$  is hydrogen;

$R_7$  and  $R_8$  are each independently:

hydrogen or

alkyl, or

$R_7$  and  $R_8$  together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

$R_{12}$  is:

hydrogen,

halo or

$C_1 - C_4$  alkyl;

$R_{13}$  is independently:

cyano,

nitro,

halo,

alkyl,  
(D)-C(O)-heterocyclyl,  
(D)-N(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>COR<sub>15</sub>,  
(D)-NR<sub>15</sub>CON(R<sub>15</sub>)<sub>2</sub>,  
(D)-NR<sub>15</sub>C(O)OR<sub>15</sub> or  
(D)-NR<sub>15</sub>SO<sub>2</sub>R<sub>15</sub>;

each R<sub>14</sub> is independently:

hydrogen,  
halo,  
alkyl,  
alkoxy or  
phenyl;

each R<sub>15</sub> is independently:

hydrogen,  
halo,  
alkyl,  
alkoxy or  
phenyl;

X is:

alkyl,  
(D)-cycloalkyl,  
(D)-heterocyclyl,  
(D)-NHC(O)R<sub>17</sub> or  
(D)-CON(R<sub>17</sub>R<sub>17</sub>);

Y is:

hydrogen,  
alkyl,  
(D)-cycloalkyl or  
(D)-heterocyclyl;

Cy is

aryl or

5- or 6-membered heteroaryl;

Cy' is benzene;

D is a bond or CH<sub>2</sub>;

M is NSO<sub>2</sub>R<sub>18</sub>;

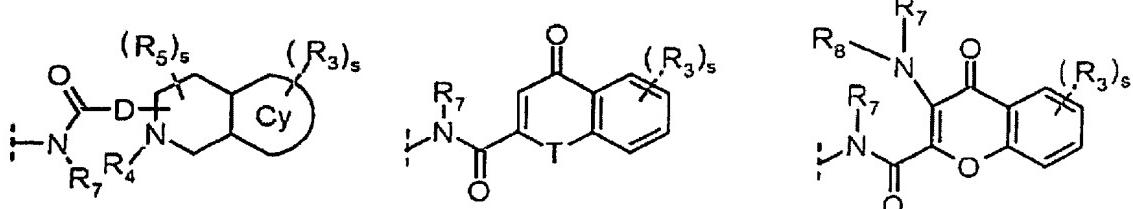
G is D;

s is 0 or 1.

4. (Currently Amended) The compound of ~~any of claims 1 to 3~~ claim 1, wherein

R<sub>1</sub> is (CH<sub>2</sub>)-phenyl or (CH<sub>2</sub>)-naphthyl which may be substituted with one to three halo atoms;

R<sub>2</sub> is:



R<sub>12</sub> is hydrogen;

R<sub>13</sub> is independently:

cyano,

nitro,

halo or

(D)-NR<sub>15</sub>COR<sub>15</sub>;

X is:

C<sub>1</sub> - C<sub>4</sub> alkyl,

C<sub>5</sub> - C<sub>7</sub> cycloalkyl,

(D)-CON(R<sub>17</sub>R<sub>17</sub>) or  
N-containing heterocyclyl;

Y is:

hydrogen,  
C<sub>1</sub> - C<sub>4</sub> alkyl or  
C<sub>5</sub> - C<sub>7</sub> cycloalkyl;

Cy is aryl;

G is CH<sub>2</sub>.

5. (Currently Amended) ~~The compound of any of claims 1 to 4 for use as a medicament comprising the compound of claim 1.~~

6. (Currently Amended) ~~Use of the compound of any of claims 1 to 4 for the preparation of a medicament for the treatment or prevention of~~ A method of treating or preventing disorders, diseases or conditions responsive to the modulation of the melanocortin-4 receptor in a mammal, where modulation means activation in the case of MC4-R agonists or inactivation in the case of MC4-R antagonists, the method comprising administering to a human or mammal an effective amount of the compound of claim 1.

7. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of cancer cachexia.~~ A method of treating or preventing cancer cachexia, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

8. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of muscle wasting.~~ A method of treating or preventing muscle wasting, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

9. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anorexia.~~ A method of treating or preventing anorexia, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

10. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anxiety and/or depression.~~ A method of treating or preventing anxiety and/or depression, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

11. (Currently Amended) ~~Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of obesity.~~ A method of treating or preventing obesity, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

12. (Currently Amended) ~~Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of diabetes mellitus.~~ A method of treating or preventing diabetes mellitus, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

13. (Currently Amended) ~~Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of male or female sexual dysfunction.~~ A method of treating or preventing male or female sexual dysfunction, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

14. (Currently Amended) ~~Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of erectile dysfunction.~~ A method of treating or preventing erectile dysfunction, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

15. (Currently Amended) A pharmaceutical composition which comprises a compound  
~~of any of claims 1 to 4~~claim 1 and a pharmaceutically acceptable carrier.